

broadened out by extremely rapid exchange with solvent oxygen.

We interpret the increase of line width with temperature as being due to chemical exchange, and since there is no direct evidence of other species with which exchange can take place, we attribute the increase primarily to exchange with the oxygens of the solvent, with a room-temperature rate constant of about 10^3 s⁻¹. Since the form of the rate law for exchange has not been established, this is an overall pseudo-first-order rate constant. It applies to the rate for exchange of all of the slowly exchanging oxygen atoms in the Np(VII) moiety.²⁰

The kinetic parameters given in Table II appear to differ significantly between the two solutions that were studied. An obvious difference between these two solutions is that the 0.5 M NaOH solution contained very much less Np(VI) than did the solution prepared by simply dissolving "Li₅NpO₆" in water. This is due partly to the ozonation of the NaOH solution, but probably more to the limited solubility of Np(VI) in 0.5 M NaOH. The rate of exchange appears to be significantly greater in the solution without NaOH, and it is possible that this increase results from an oxygen exchange between Np(VII) and Np(VI). It is interesting that $1/T^{\circ}_2$ is larger in the 0.5 M NaOH solution; i.e., the "intrinsic" line width in the absence of exchange is greater in such solutions. The crudeness of our kinetic analysis and the limited range of Np(VII) and base concentrations over which measurements can be made make it appear unprofitable to pursue these effects in greater detail or to attempt to deduce a complete rate

law. In any case, the difference in parameters between the two solutions can be regarded as setting an upper limit to the rate of any Np(VI)–Np(VII) exchange.

It is noteworthy that we see no evidence of an Np(VI) oxygen resonance in the solution made by dissolving "Li₅NpO₆" in water, even though substantial amounts of Np(VI) are present. An Np(VI) oxygen resonance has been observed in acid solution about 2900 ppm downfield of the solvent,²¹ and we have seen a similar resonance in carbonate solutions containing Np(VI). These observations would suggest that the Np(VI) oxygen resonance is broadened out in strongly alkaline solution, presumably by rapid exchange with solvent oxygen. (If Li₅NpO₆ dissolves to form NpO₄(OH)₂³⁻, the resulting solution will necessarily be strongly alkaline, since it will contain two free hydroxide ions per neptunium.)

Acknowledgment. We wish to thank Robert Botto, James Norris, and Arthur Thompson for discussions relating to the NMR measurements and data manipulation. Dominique Martin-Rovet of CNRS, Saclay, France, carried out the synthesis of Li₅NpO₆ in our laboratory, and we thank Lester Morss for his help in optimizing this synthesis. We are further pleased to acknowledge helpful discussions with Professors Robert E. Connick and R. Kent Murmann. We thank an anonymous reviewer for calling our attention to ref 20.

Registry No. NpO₄(OH)₂³⁻, 44442-28-6; Np, 7439-99-8.

(20) Swaddle, T. W. *Adv. Inorg. Bioinorg. Mech.* **1983**, *2*, 121.

(21) Shcherbakov, V. A.; Mashirov, L. G. *Radiokhimiya* **1984**, *26*, 703.

Notes

Contribution from the Department of Chemistry,
Princeton University, Princeton, New Jersey 08544

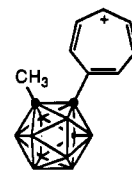
A Carbon-to-Boron-Bridged Benzo-*o*-carborane

Shao-hai Wu* and Maitland Jones, Jr.*

Received October 27, 1987

The electronic structure of hypervalent carbon has greatly interested chemists from very different fields, including organometallic, carborane, and cluster (carbide) chemistry, as well as carbocation chemistry.¹ Hypervalent carbon atoms are generally found in electron-deficient systems, where electrons are in short supply and thus have to be spread relatively thinly to hold molecules or ions together. Although the concepts of three-center-two-electron or multicenter bonding, pioneered by Lipscomb,² have been a great help in this area, the local bonding structures of some hypercarbons still puzzle chemists. This is especially true in icosahedral carborane chemistry. The organic chemistry of carboranes developed during the past two decades is largely confined to the carbons in the cage, and the number of these carbon-substituted carboranes, which include metallocarboranes containing carbon–metal bonds, has been ever growing.³ Nevertheless, the electronic bonding structure of the two cage carbons in these molecules still remains ambiguous.

The theoretical treatment of icosahedral carboranes can be traced to early work by Hoffmann and Lipscomb in the 1960s.⁴ Their elegant prediction of "superaromaticity" of carboranes has been successfully verified by experimental chemists.³ Since the 1960s, carboranes have been often described as three-dimensional aromatic compounds in analogy to the two-dimensional benzene rings.³ The demonstration of conjugation between a p orbital on a π substituent attached to the cage and a surface orbital of the polyhedron, as suggested by Hoffmann and Lipscomb,⁴ however, has proven to be much more difficult. The measurements, by Hawthorne, Berry and Wegner,⁵ of pK_a's for carboranylbenzoic acids and carboranylaminium ions, and of ¹⁹F NMR chemical shifts of carboranylfluorobenzenes, showed that the -I effect of the *o*-carborane cage is similar in magnitude to that of the halogens, and that ground-state cage–ring π interaction is *not* important.⁵ These authors also found that isomer ratios in nitration of 1-phenylcarborane (*o:m:p* = 4:26:70) indicate electron donation by the cage in the transition state for nitration.⁵ However this +*T* effect could not be observed when UV and ¹H NMR spectra of the 1-methyl-2-tropenylmethylcarborane cation **1** were studied.⁶



1

The results from UV and Raman spectra of phenylcarboranes

- (1) Olah, G. A.; Prakash, G. K. S.; Williams, R. E.; Field, L. D.; Wade, K. *Hypercarbon Chemistry*; Wiley-Interscience: New York, 1987.
- (2) Lipscomb, W. N. *Advances in Inorganic Chemistry and Radiochemistry*; Academic: New York, 1959; Vol. I, p 117 and references therein. Lipscomb, W. N. *Boron Hydrides*; Benjamin: New York, 1963.
- (3) *Boron Compounds, Gmelin Handbook of Inorganic Chemistry*; Springer-Verlag: West Berlin, 1981; 1st supplement, Vol. 3 and earlier volumes. Grimes, R. N. *Carboranes*; Academic: New York, 1970. Grimes, R. N. *Metal Interactions with Boron Clusters*; Plenum: New York, 1982.

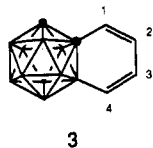
- (4) Hoffmann, R.; Lipscomb, W. N. *J. Chem. Phys.* **1962**, *36*, 2179. Hoffmann, R.; Lipscomb, W. N. *J. Chem. Phys.* **1962**, *36*, 3489.
- (5) Hawthorne, M. F.; Berry, T. E.; Wegner, P. A. *J. Am. Chem. Soc.* **1965**, *87*, 4746.
- (6) Harmon, K. M.; Harmon, A. B.; Thompson, B. C. *J. Am. Chem. Soc.* **1967**, *89*, 5309.

similarly indicated that the carborane nucleus essentially does *not* change the system of π -electron levels of an attached benzene ring, apparently manifesting only an inductive effect.⁷

Hota and Matteson approached the problem in a different way. They synthesized the carbon-to-carbon bridged benzo-*o*-carborane **2**,⁸ in which two different delocalized bonding systems are fused; the exo "benzene" ring shares a C-C edge with the icosahedral



carborane nucleus. It was thought that, in molecule **2**, the orbitals of the icosahedron could be factored in such a way that the two "hypercarbon" atoms would have p orbitals properly oriented to complete the π system of the benzenoid ring. Thus the authors asked "whether the stability of the benzenoid π -bond system would be sufficient to overcome the resistance of the *o*-carborane toward external conjugation and result in measurable aromatic character in the carbocyclic ring".⁸ Unfortunately, their results do not clarify the situation completely because it was extremely difficult to differentiate the inductive effect of the cage from any resonance effects. The lack of chemical reactivity of **2** toward electrophilic reagents like sulfuric acid and bromine, although consistent with aromaticity, could be the result of the strong electron-withdrawing influence of the icosahedral cage together with steric effects. Only the ¹H NMR spectrum of **2** provides tenuous evidence of aromatic behavior. Even here the chemical shift of the ring protons is at most only 0.2–0.3 ppm⁸ downfield from that expected of a diene. Because the two carbon atoms in an icosahedral carborane cage possess some positive charge^{4,9–11} and therefore are the most electron-withdrawing centers in the system, it occurred to us that molecule **3**, a carbon-to-boron-bridged benzo-*o*-carborane, might



serve as a critical test to probe the induction vs resonance problem. As shown in the following discussion, if the inductive effect of the icosahedral carborane nucleus in **3** predominates and there were no measurable π conjugation between the two electron-delocalized systems, one would expect to see the chemical shifts of the ring protons in **3** shifted upfield relative to those of **2**. One would further expect that the proton adjacent to the cage carbon atom, H₁, would show a downfield shift relative to the proton adjacent to the cage boron atom, H₄. In this paper, we report the synthesis of **3** and discuss its NMR spectra.

Results and Discussion

Recently¹² we described the reaction of carbomethoxycarbene with the B-H bonds of *o*-carborane to form the products of formal B-H insertion. We have used an intramolecular version of this

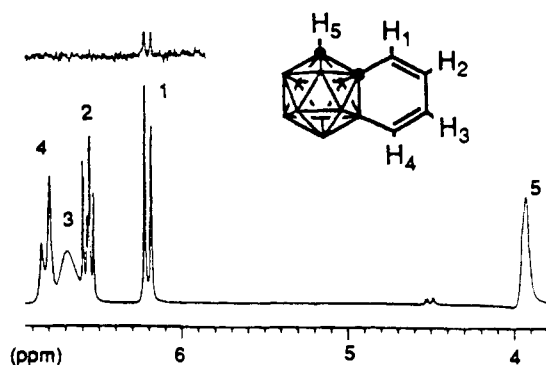
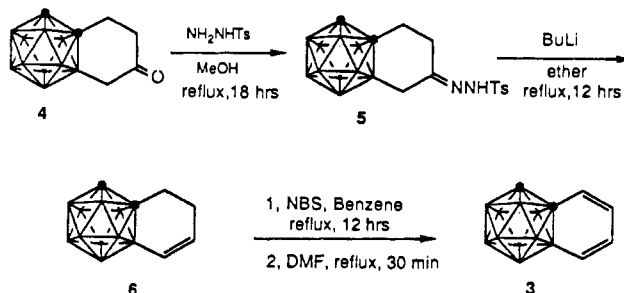


Figure 1. ¹H NMR spectrum (250 MHz) of **3** in CDCl₃ at 298 K. Inset: Irradiation (NOE difference) at 3.94 ppm (cage C-H) resulted in signal enhancement at only one (H₁, δ = 6.21) of the four ring protons.

reaction to produce a series of carbon-to-boron-bridged *o*-carboranes.¹³ Thus the six-membered-ring ketone **4** has been made in 20–30% isolated yield based on the corresponding acid chloride.¹⁴ The X-ray structure verified our earlier assignment, and showed that attachment of the ring was at the 4,5-boron, and not at the other sterically accessible position (3,6).¹⁵ Ketone **4** was converted to tosylhydrazone **5**. Compound **5** was then reduced with *n*-butyllithium in THF at 0 °C, followed by refluxing for 8 h, to give a major product **6** (when the reaction was run at room temperature for 3 h, a second isomer **7** was also isolated in nearly equal amounts). The crude product of bromination of **6** with *N*-bromosuccinimide in benzene was refluxed in dimethylformamide (DMF) for 1/2 h to give **3**, which was purified by preparative gas chromatography, in about 10–20% yield (colorless oil). Precise mass spectrometry revealed the molecular formula of **3** to be C₆B₁₀H₁₄. The ultraviolet spectrum of **3** has the strongest absorption at λ_{\max} 266 nm (ϵ_{\max} 4700), which is very similar to that of **2**, λ_{\max} 260 nm (ϵ_{\max} 2950).⁸

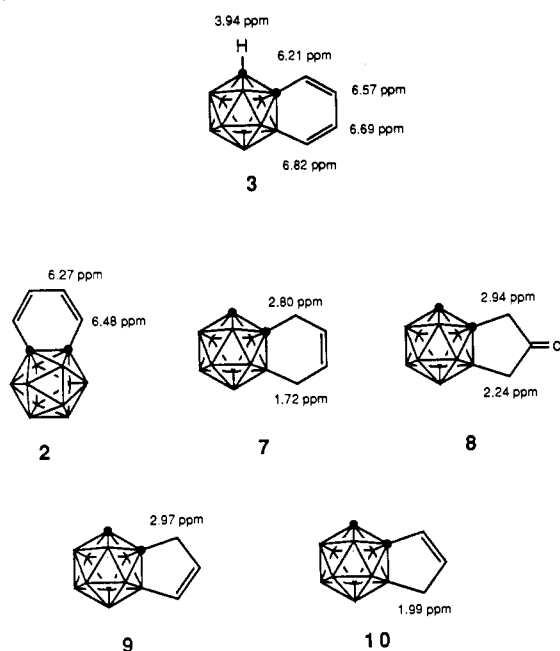


The ¹H NMR spectrum of **3** with its chemical shift assignment is shown in Figure 1. The sharp doublet at 6.21 ppm was assigned to proton H₁, adjacent to the cage carbon, as this is the only peak that shows an Overhauser effect when the remaining cage C-H₅ (3.94 ppm) is irradiated. Proton decoupling shows that H₁ is coupled to H₂ (6.57 ppm). H₃ (6.69 ppm, br m) and H₄ (6.82 ppm, br d) were assigned by their coupling patterns. For comparison, relevant chemical shifts of compounds **2**,⁸ **7**,⁸ **8**,¹³ **9**,¹³ and **10**¹³ are also shown in Chart I. It can be seen that the average chemical shift of the ring protons in **3** (6.57 ppm), shows a downfield shift relative to **2**, whose corresponding average chemical shift is 6.37 ppm. In addition, it is interesting to note that, in **3**, proton H₄, adjacent to the bridged boron atom, is shifted 0.61 ppm downfield from proton H₁, adjacent to the cage carbon. These results are in sharp contrast to the picture that one may expect to see on the assumption that the icosahedral cage withdraws electrons inductively, with no resonance effect.^{5–8} As we have mentioned before, the two carbon atoms in the icosahedral carboranes are the most electron-withdrawing centers. Numerous

- (7) Leites, L. A.; Vinogradova, L. E.; Kalinin, V. N.; Zakharkin, L. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1970**, 2596.
 (8) Hota, N. K.; Matteson, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 3570. Hota, N. K.; Matteson, D. S. *J. Am. Chem. Soc.* **1971**, *93*, 2893.
 (9) Dixon, D. A.; Kleier, D. A.; Halgren, T. A.; Hall, J. H.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1977**, *99*, 6226. Cheung, C. S.; Beaudet, R. A.; Segal, G. A. *J. Am. Chem. Soc.* **1970**, *92*, 4158. Dewar, M. J. S.; McKee, M. L. *J. Am. Chem. Soc.* **1980**, *102*, 2662.
 (10) Shatenshtein, A. I.; Zakharkin, L. I.; Petrov, E. S.; Yakouleva, E. A.; Yakoshin, F. S.; Vukmirovich, Z.; Isaeva, G. G.; Kalinin, V. N. *J. Organomet. Chem.* **1970**, *23*, 313.
 (11) Laubengayer, A. W.; Rysz, W. R. *Inorg. Chem.* **1965**, *4*, 1513. Marnca, R.; Schroeder, H. A.; Laubengayer, A. W. *Inorg. Chem.* **1967**, *6*, 572. Echeistova, A. I.; Syrkin, Y. K.; Stanko, V. I.; Klimova, A. I. *Zh. Strukt. Khim.* **1967**, *8*, 933.
 (12) Zheng, G.; Jones, M., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 6487.

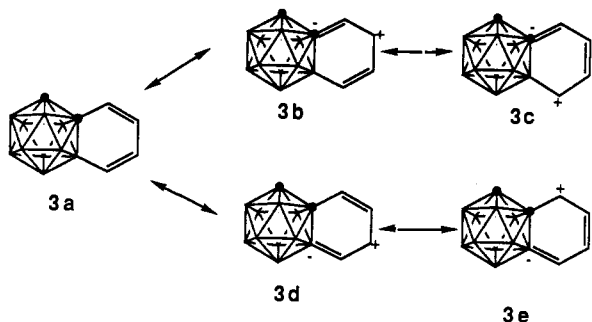
- (13) Wu, S.; Jones, M., Jr. *Inorg. Chem.* **1986**, *25*, 4802.
 (14) The synthetic procedure for **4** has been slightly changed from that of ref 13. α, α, α -Trifluorotoluene was found to be a better solvent than toluene. Reaction of the carbene with solvent is reduced.
 (15) Wu, S.; Van Engen, D.; Jones, M., Jr., unpublished work.

Chart I



calculations^{4,9} suggest that the carbon atoms in carboranes are positively charged because of the tendency of the carbon to donate electrons into the electron-deficient boron system. This has been reflected by both pK_a data¹⁰ of the cage C–H protons and the dipole moments¹¹ of carboranes. Therefore the “hypercarbon” atoms can be expected to withdraw electrons from attached groups outside the cage. This is illustrated by the chemical shift behavior of their attached protons. The methylene groups attached to the cage carbons in **7** and **8** are shifted downfield relative to the methylene group attached to the cage borons. Similarly, the methylene protons attached to the cage carbon in **9** are shifted downfield relative to the methylene protons attached to the cage boron in **10**. However, a completely reversed picture appears in **3**. It seems clear that the inductive effect of the icosahedral carboranes in **3** fails to account for this NMR phenomenon, and the assumption that there is no measurable π conjugation between the cage and its substituents, as suggested by earlier work, may not be valid for **3**.

We believe that cage–ring π conjugation may play an important role. The connection of p orbitals of the ring with p-type surface orbitals of the icosahedral cage should give rise to a series of resonance structures, **3a–e**. Because the cage carbon atoms in



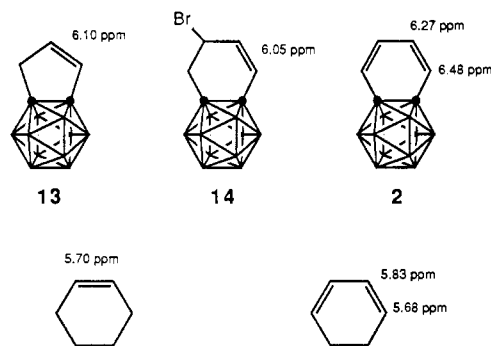
carboranes are partially positively charged, they should be better electron acceptors than the cage borons, not only for σ electrons, which has been illustrated by the strong inductive effect, but also for π electrons. It is then likely that **3b** and **3c** are more important resonance contributors than **3d** and **3e**. In accord with the notion that **3c** is the most stable of the four charge-separated resonance structures, H_4 shows the largest downfield shift. We conjecture that the cage boron, which is partially negatively charged, may somewhat stabilize the positive charge on the adjacent ring position (**3c**).

In 1981 Hutton, Roth, and Chari¹⁶ reported the triplet EPR spectra of *o*-carboranylcarbenes **11** and **12** observed at 5 K. They

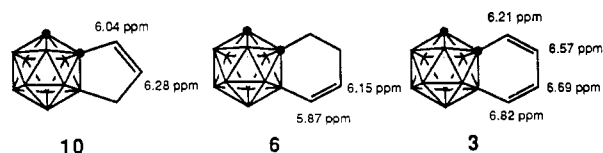


found that there was little, but not zero, delocalization of π -spin density into the carboranyl cage. The lack of efficient delocalization of spin density was attributed to the large energy differences between the 2p orbital of the divalent carbon and the highest occupied and the lowest unoccupied molecular orbitals of the carborane cage.¹⁶ Similar arguments have been proposed to account for the failure to observe conjugation between a p orbital on a π substituent and the surface orbital of the icosahedral carboranes.⁸ However, evidence for apical–apical conjugation through the $B_{10}H_{10}^{2-}$ system has also been reported for the compound in which a diazonium group, a π -electron acceptor, was attached to the para position relative to electron-donor substituents like amino groups.¹⁷ Another related feature of carboranes is the NMR antipodal shifts induced by substituents. A range of groups attached to boranes and heteroboranes produces distinct NMR chemical shifts at the cage atom para to the point of substitution.¹⁸ Although the detailed mechanism of this “para” effect has not been completely explained, it is very likely that resonance must be involved.¹⁹ Our work provides new evidence that, by properly choosing the model molecule, cage–ring π conjugation can be demonstrated.

In ref 8, Hota and Matteson raised the question of aromaticity of the exo ring in **2**, and attributed the 0.2–0.3 ppm downfield shift of the exo ring protons to ring current. This value was obtained by comparison of **2** with carboranes **13** and **14**.⁸ The real number attributed to ring current in **2** could be even smaller than 0.2–0.3 ppm if one included the influence of a second vinyl group. For example, the chemical shift difference between the vinyl protons in cyclohexene (5.70 ppm) and in cyclohexadiene (average at 5.76 ppm) is about 0.06 ppm. A similar comparison



can be made for molecule **3**. Here in spite of a big downfield shift (0.95 ppm) of H_4 (6.82 ppm) in **3** relative to that (5.87 ppm) in **6**, a difference of only 0.17 ppm was found between H_1 (6.21 ppm) in **3** and that (6.04 ppm) in **10**.¹³ Therefore, although there is



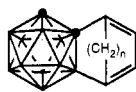
(16) Hutton, R. S.; Roth, H. D.; Chari, S. *J. Phys. Chem.* **1981**, *85*, 753.

(17) Knoth, W. H. *J. Am. Chem. Soc.* **1966**, *88*, 935.

(18) For example, see: Stanko, V. I.; Babushkina, T. A.; Klimova, T. P.; Gol'tyapin, Yu. V.; Klimova, A. I.; Vasil'ev, A. M.; Alymov, A. M.; Khrapov, V. V. *Zh. Obshch. Khim.* **1976**, *46*, 1071 and references therein.

(19) Hermánek, S.; Plešek, J.; Gregor, V.; Stíbr, B. *J. Chem. Soc., Chem. Commun.* **1977**, 561.

π conjugation between the cage and the ring, the poor p-type surface orbital overlap in the fused C–B edge in **3** makes a ring current unlikely. In other words, π conjugation between the ring and the cage through the bridged “hypercarbon” atom does not necessarily lead to aromaticity of the exo ring in **3**. A crucial test might be the observation of an induced upfield shift in the bridge protons of the as yet unknown carborane **15**.



15

Experimental Section

General Remarks. ^1H NMR spectra were recorded on a Bruker WM250 spectrometer at 250 MHz in CDCl_3 , with signals referenced to Me_4Si . ^{11}B NMR spectra were recorded on a Bruker WM250 spectrometer (80 MHz for ^{11}B) in CDCl_3 , with signals referenced to external boron trifluoride etherate. Chemical shifts were measured on decoupled spectra and multiplicities on coupled spectra. Ultraviolet and visible spectra (UV) were taken with a Hewlett Packard 8450A spectrophotometer. Analytical gas chromatography was performed on a Hewlett-Packard 5890A gas chromatograph with helium as carrier gas, using 2-mm-i.d. stainless-steel columns. GC/MS runs were conducted on a Hewlett-Packard 5992B instrument, using packed 2-mm-i.d. glass columns. Preparative gas chromatography was performed on a Varian A90A gas chromatograph with helium as carrier gas, using a $1/4$ -in. by 4-ft aluminum column packed with 15% OV-101 on 80/100 Chromosorb W-HP. Mass spectra were obtained on a KRATOS MS 50 RFA high-resolution mass spectrometer. In general, reactions were conducted under an inert atmosphere of argon. All solvents were purified and dried by using standard procedures.

Preparation of 6. To a solution of **4** (1 g, 0.005 mol) in methanol (25 mL) was added *p*-toluenesulfonic acid hydrazide (0.93 g, 0.005 mol). The mixture was refluxed for 12 h. The methanol was removed. The resulting gummy mass was triturated with dry pentane to remove the residual methanol. A yellow sticky solid (1.65 g) was obtained for further reaction.

The crude product (1 g, about 2.5 mmol) was dissolved in freshly distilled dry THF (30 mL). *n*-Butyllithium (3 mL, 2.5 M in hexane; 7.5 mmol) was added by a syringe to the THF solution under argon flow at 0 °C. The solution was refluxed for 8 h and cooled. The reaction mixture was quenched with water, the organic layer was separated, and the aqueous layer was extracted with four 50-mL portions of ether. The combined organic extracts were washed with a saturated sodium bicarbonate solution and dried over magnesium sulfate, and the solvent was removed. The residual material was vacuum-distilled by a Kugelrohr apparatus (150 °C; 0.1 Torr) to yield 200 mg (40%) of slightly yellow oil. This sample (with 95% purity by GC) was suitable for preparation of **3**. Further purification by preparative GC provided analytical sample of **6**, a colorless oil. ^1H NMR (CDCl_3): δ 6.15 (br m, 1 H), 5.87 (br d, 1 H, $J = 13.2$ Hz), 3.63 (br s, 1 H), 2.52–2.19 (m, 4 H). ^{11}B NMR (CDCl_3): δ -3.7 (d, 2 B), -7.6 (d, 2 B), -9.7 (s, 1 B), -10.8 to -13.2 (d, 3 B), -15.1 (d, 1 B), -16.2 (d, 1 B).

When the reaction was run at room temperature for 3 h, a second isomer **7** was also isolated in about equal yield. ^1H NMR (CDCl_3): δ 5.88 (br m, 1 H), 5.45 (br m, 1 H), 3.66 (br s, 1 H), 2.80 (AB quartet, 2 H), 1.72 (br m, 2 H).

Preparation of 3. To a solution of **6** (60 mg, 0.31 mmol) in dry benzene (8 mL) was added *N*-bromosuccinimide (60 mg, 0.34 mmol) and a catalytic amount of benzoyl peroxide. The mixture was refluxed under argon flow for 12 h. The benzene was removed. The residual material was dissolved in dimethylformamide (3 mL) and then was heated rapidly to reflux for 0.5 h. The solution was cooled and diluted with 20 mL of pentane and washed with 10 mL of water. The organic layer was extracted with four 20-mL portions of pentane. The combined pentane solutions were washed with water and concentrated. Preparative GC yielded an analytical sample of **3** (7.4 mg, 13%; colorless oil). Precise mass for $\text{B}_{10}\text{C}_6\text{H}_{14}$: calcd, 194.2885; found, 194.2091. UV (CDCl_3), λ_{max} (ϵ): 266 nm (4700), 274 nm (4000). ^1H NMR (CDCl_3): δ 6.82 (br d, 1 H, $J = 12.4$ Hz), 6.69 (br m, 1 H), 6.57 (ddd, 1 H, $J = 9.7, 6.1, 1.2$ Hz), 6.21 (d, 1 H, $J = 9.8$ Hz), 3.94 (br s, 1 H). ^{11}B NMR (CDCl_3): δ -3.1 (d, 1 B), -9.7 (s, 1 B; d, 2 B), -12.9 (d, 2 B), -15.0 (d, 2 B), -17.0 (d, 1 B), -18.5 (d, 1 B).

Acknowledgment. Support by the National Science Foundation through Grants CHE 83-18345 and 86-17590 is gratefully acknowledged. We thank the Department of the Army for a generous supply of decaborane. Our thanks also go to Mary W. Baum

for her expert help with the NMR spectroscopy and to Dr. J. E. Jackson for helpful comments upon the manuscript.

Registry No. **3**, 113860-56-3; **4**, 105335-31-7; **5**, 113860-54-1; **6**, 113860-55-2; **7**, 113860-57-4.

Contribution from the Department of Chemistry,
University of Wyoming, Laramie, Wyoming 82071

Calcium Binding to γ -Carboxyglutamate and β -Carboxyaspartate Residues: Structure of a Calcium Complex of Benzylmalonic Acid

Yoshinobu Yokomori¹ and Derek J. Hodgson*

Received October 23, 1987

The presence of the modified amino acid residues γ -carboxyglutamic (Gla) and β -carboxyaspartic (Asa) acids in a variety of proteins is well documented,^{2–6} and it is well established that Gla residues are implicated in calcium binding in both blood and bone proteins.⁷ Since several authors have suggested that a principal role for Gla is in the discrimination between calcium and magnesium,⁸ we and others have been investigating the structures of a variety of model complexes designed to probe the modes of binding of calcium, magnesium, and related metals to Gla and/or Asa.^{9–12}

The bonding patterns of relevant metals to carboxylate moieties have been reviewed by Einspahr and Bugg,¹³ who note that for a monocarboxylate functionality (as in Glu or Asp) a metal can bind in either a unidentate or a bidentate fashion. The unidentate mode involves metal coordination to a single oxygen atom, while the bidentate form involves metal ion binding to both oxygen atoms of a single carboxylate group. In a dicarboxylate like Gla or Asa, however, a third binding mode is possible; in this mode the metal again binds to two oxygen atoms, but the two oxygen atoms are from different carboxylates. This mode of binding is usually referred to as the “malonate” mode since it is available only to a dicarboxylate like malonate (or Gla or Asa).

No definitive crystallographic study of a metal complex of either Asa or Gla has been published, but we and others have modeled these residues by the use of α -substituted malonate derivatives.^{9–12} Thus, in recent years the modes of binding of calcium to α -ethylmalonate⁹ and α -methylmalonate¹⁰ have been reported, as have the interactions between magnesium and α -methylmalonate¹⁰ and those between barium and several substituted malonates.¹²

- (1) Present and permanent address: Department of Chemistry, The National Defense Academy, Hashirimizu, Yokosuka 239, Japan.
- (2) Magnusson, S.; Sottrup-Jensen, L.; Peterson, T. E.; Morris, H. R.; Dell, A. *FEBS Lett.* **1974**, *44*, 189–193.
- (3) Stenflo, J.; Fernlund, P.; Egan, W.; Roepstorff, P. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 2730–2733.
- (4) Prendergast, F. G.; Mann, K. G. *J. Biol. Chem.* **1977**, *252*, 840–850.
- (5) Lian, J. B.; Hauschka, P. V.; Gallop, P. M. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* **1978**, *37*, 2615–2620.
- (6) Christy, M. R.; Barkley, R. M.; Koch, T. H.; Van Buskirk, J. J.; Kirsch, W. M. *J. Am. Chem. Soc.* **1981**, *103*, 3935–3937. Christy, M. R.; Koch, T. H. *J. Am. Chem. Soc.* **1982**, *104*, 1771–1772.
- (7) Jackson, C. M.; Nemerson, Y. *Annu. Rev. Biochem.* **1980**, *49*, 765–811.
- (8) Williams, R. J. In *Calcium Binding Proteins and Calcium Function*; Wasserman, R. H., et al., Eds.; Elsevier: New York, 1977; pp 1–12.
- (9) Zell, A.; Einspahr, H.; Bugg, C. E. *Biochemistry* **1985**, *24*, 533–537.
- (10) Curry, M. E.; Eggleston, D. S.; Hodgson, D. J. *J. Am. Chem. Soc.* **1985**, *107*, 8234–8238.
- (11) Eggleston, D. S.; private communication.
- (12) Yokomori, Y.; Flaherty, K. A.; Hodgson, D. J. *Inorg. Chem.*, in press.
- (13) Einspahr, H.; Bugg, C. E. *Acta Crystallogr., Sect., B: Struct. Crystallogr. Cryst. Chem.* **1981**, *B37*, 1044–1052.